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BRIEF AND ADDENDUM FOR APPELLEE - DIRECTOR OF THE UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

Appeal No. 03-1327
Serial No. 08/485,129

IN RE DAVID WALLACH, HARTMUT ENGELMANN, DAN ADERKA, DANIELA NOVICK AND MENACHEM RUBINSTEIN

APPEAL FROM THE UNITED STATES PATENT AND TRADEMARK OFFICE,
BOARD OF PATENT APPEALS AND INTERFERENCES

JOHN M. WHEALAN
Solicitor

MARY L. KELLY
RAYMOND T. CHEN
Associate Solicitors

P.O. Box 15667
Arlington, Virginia 22215
(703) 305-9035

Attorneys for the Director of the United States Patent and Trademark Office

September 30, 2003

Representative Claim

11. An isolated DNA molecule comprising a contiguous nucleotide sequence coding for a protein consisting of naturally occurring human Tumor Necrosis Factor (TNF) Binding Protein II, herein designated TBP-II, said TBP-II including the amino acid sequence: Thr-Pro-Tyr-Ala-Pro-Glu-Pro-Gly-Ser-Thr in the portion of the protein sequenced by N-terminal sequence analysis, said protein having the ability to inhibit the cytotoxic effect of TNF, wherein said naturally occurring TBP-II protein is the same as that protein having the ability to inhibit the cytotoxic effect of TNF which, after being purified by subjecting a crude protein recovered from a dialyzed concentrate of human urine to affinity chromatography on a column of immobilized TNF, elutes from a reversed-phase high pressure liquid chromatography column as a single peak in a fraction corresponding to about 31% acetonitrile and shows a molecular weight of about 30 kDa when measured by SDS-PAGE under reducing conditions.

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STATEMENT OF RELATED CASES

The Director is not aware of any other appeal from the Board of Patent Appeals and Interferences in connection with patent application U.S. Serial No. 08/485,129 that has previously been before this or any other court. There is no known related case pending in this or any other court. The Director is also unaware of any other cases pending in this or any other court that will directly affect or be directly affected by this Court's decision in the pending appeal.

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I. STATEMENT OF THE ISSUE

Representative claim 11 is directed to a broad genus of DNA molecules that, if issued, would cover every one of the millions of DNA molecules capable of encoding the TBP-II protein. However, Wallach's specification does not teach the complete nucleic acid sequence of a single DNA molecule within the broad genus of DNA molecules Wallach claims. Likewise, Wallach's specification does not teach the complete amino acid sequence of the TBP-II protein encoded by the claimed DNA molecules. Instead, Wallach's specification discloses only the sequence of ~7% of the 195-202 amino acids that make up the full-length TBP-II protein. Further,

Wallach's specification does not teach any function of the claimed DNA molecules except the naked recitation that they encode the TBP-II protein. Wallach's specification fails to provide any other information from which the claimed DNA molecules might be distinguished from other DNA molecules. Because of these deficiencies, the Board found that Wallach's specification lacks adequate written support for the broadly claimed genus of DNA molecules encompassed by representative claim 11. Thus, the sole issue on appeal is whether substantial evidence supports the Board's factual finding that Wallach's specification does not describe the claimed genus of DNA molecules in the manner required by 35 U.S.C. § 112, first paragraph.

II. STATEMENT OF THE CASE

This is an appeal from a decision of the Board of Patent Appeals and Interferences (the "Board") of the United States Patent and Trademark Office ("USPTO") affirming the final rejection of claims 11-13, 35-38, 43-44, 46-49, 51-54, 56-61, and 63-64 of U.S. Serial No. 08/485,129 ("Wallach's specification") under 35 U.S.C. § 112, first paragraph, for lack of written description. A1-A11.[1] The appellants (hereinafter "Wallach") have stated before the Board that all claims on

[1] Citations to Appellants' Brief will be referred to as "Appellants' Br. at __," and citations to the Joint Appendix as "A__."

2nd position of codon

1st position of codon (5′ terminus)	U	C	A	G	3rd position of codon (3′ terminus)
U	UUU Phe	UCU Ser	UAU Tyr	UGU Cys	U
	UUC Phe	UCC Ser	UAC Tyr	UGC Cys	C
	UUA Leu	UCA Ser	UAA Stop (Ochre)	UGA Stop	A
	UUG Leu	UCG Ser	UAG Stop (Amber)	UGG Trp	G
C	CUU Leu	CCU Pro	CAU His	CGU Arg	U
	CUC Leu	CCC Pro	CAC His	CGC Arg	C
	CUA Leu	CCA Pro	CAA Gln	CGA Arg	A
	CUG Leu	CCG Pro	CAG Gln	CGG Arg	G
A	AUU Ile	ACU Thr	AAU Asn	AGU Ser	U
	AUC Ile	ACC Thr	AAC Asn	AGC Ser	C
	AUA Ile	ACA Thr	AAA Lys	AGA Arg	A
	AUG Met	ACG Thr	AAG Lys	AGG Arg	G
G	GUU Val	GCU Ala	GAU Asp	GGU Gly	U
	GUC Val	GCC Ala	GAC Asp	GGC Gly	C
	GUA Val	GCA Ala	GAA Glu	GGA Gly	A
	GUG Val	GCG Ala	GAG Glu	GGG Gly	G

The Genetic Code

appeal "stand or fall together." A4-A5; *see also* Appellants' Br. at 10, ¶2. Accordingly, this appeal is directed to representative claim 11.

III. STATEMENT OF THE FACTS

A. The Technology[2]

DNA is made up of nucleic acids (*i.e.*, G, A, T and C) linked together like beads on a string. Proteins are made up of a different kind of chemicals called amino acids (*e.g.*, alanine, glutamine, etc.) that are similarly linked together like beads on a string. DNA "encodes" (or "codes for") the order and type of amino acids that make up a given protein. More specifically, the DNA that encodes a protein can be divided into groups of 3 nucleic acids (or nucleotides) called "codons." When a protein is synthesized, parts of a cell "read" each 3 nucleic acid codon, and build a protein by adding an amino acid that corresponds to a given codon onto the end of the protein under construction. For example, the codon "AGG" codes for the amino acid arginine, so, wherever the codon AGG appears in a DNA, an arginine will be added onto the protein that DNA encodes. As shown in the Genetic Code on the facing page, more than one codon may be used to code for a particular amino acid. (*See* JOSEPH SAMBROOK & DAVID W. RUSSELL, MOLECULAR CLONING: A LABORATORY MANUAL, Nina Irwin, Ed., Vol. 3, A7.5, Cold Spring Harbor Laboratory Press (3d

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[2] For a description of the relevant technology as enunciated by this Court, see the

ed. 2001); Add. at 3.) Accordingly, several very different DNA sequences can encode the same protein. The Genetic Code also makes it is possible to predict which DNA molecules can encode a protein if the amino acid sequence of that protein is known. However, without the amino acid sequence, it is not possible to predict which DNA molecules encode a given protein and, instead, the DNA itself must be isolated and characterized.

B. The Claimed DNA Molecules

Representative claim 11 is directed to a genus of DNA molecules that encode the naturally-occurring form of Tumor Necrosis Factor ("TNF") Binding Protein II ("TBP-II"):

> 11. An isolated DNA molecule comprising a contiguous nucleotide sequence coding for a protein consisting of naturally occurring human Tumor Necrosis Factor (TNF) Binding Protein II, herein designated TBP-II,
>
> said TBP-II including the amino acid sequence: Thr-Pro-Tyr-Ala-Pro-Glu-Pro-Gly-Ser-Thr in the portion of the protein sequenced by N-terminal sequence analysis, said protein having the ability to inhibit the cytotoxic effect of TNF, wherein said naturally occurring TBP-II protein is the same as that protein having the ability to inhibit the cytotoxic effect of TNF which, after being purified by subjecting a crude protein recovered from a dialyzed concentrate of human urine to affinity chromatography on a column of immobilized TNF, elutes from a reversed-phase high pressure liquid chromatography column as a single peak in a fraction corresponding to about 31% acetonitrile and shows a

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background section of *In re Deuel*, 51 F.3d 1552, 1554 (Fed. Cir. 1995).

molecular weight of about 30 kDa when measured by SDS-PAGE under reducing conditions.

A2 (emphasis added). As illustrated above with underlining, the majority of representative claim 11 describes the TBP-II protein rather than the claimed genus of DNA molecules. For example, representative claim 11 recites that the TBP-II protein that is encoded by the claimed DNA molecules must include a specific 10 amino acid sequence at one end of the full-length TBP-II protein (*i.e.*, the N terminus). Thus, representative claim 11 addresses only the 30 nucleotide portion of the claimed DNA molecules that can be predicted to encode the first 10 amino acids of the TBP-II protein that is recited in the claims. Claim 11 provides no information about the structure of the portion of the claimed DNA molecules that encodes the other 175-182 amino acids that are estimated to make up the rest of the TBP-II protein. A383. Claim 11 is also similarly silent about the structure of any other portions of the claimed DNA molecules that might not appear in the mature, full-length TBP-II protein, but which may be necessary for proper expression of the TBP-II protein, *e.g.*, a signal sequence[3]. Thus, claim 11 recites information that can be used to predict, at most, only ~7% of the nucleic acid sequence of any DNA molecule in the claimed genus of DNA molecules.

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[3] A signal sequence is a short amino acid sequence found in many newly-synthesized proteins that determines the eventual location of the protein in the cell. A signal

Likewise, claim 11 recites no functional information about the claimed genus of DNA molecules that can be used to predict the remaining 93% of the nucleic acid sequence of any DNA molecule in the claimed genus of DNA molecules. More specifically, claim 11 is silent about the function of the claimed DNA molecules, except for the naked recitation that they code for the TBP-II protein. Further, although claim 11 recites that the TBP-II protein encoded by the claimed DNA molecules must have the same chemical and functional properties as the TBP-II protein purified from human urine, claim 11 does not correlate the recited properties of the TBP-II protein with the claimed DNA molecules.

C. Wallach's Specification

Although the claims are directed to a genus of DNA molecules that encode the TBP-II protein, Wallach's specification (A19-A71) is directed generally to the TBP-II protein, and to methods of isolating and purifying the protein from human urine. All of the working examples of Wallach's specification are limited to the TBP-II protein, *e.g.*, (i) isolating and purifying the TBP-II protein, (ii) characterizing the purified protein, (iii) producing antibodies against the purified protein, and (iv) examining the effects of anti-TBP-II antibodies and TBP-II protein on TNF activity. A37-A54. In contrast, there are no working examples in Wallach's specification

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sequence is removed from the final, mature protein during normal processing.

concerning isolating and characterizing any of the claimed DNA molecules, which encode the TBP-II protein. Instead, Wallach's specification contains only generic descriptions of how one might go about cloning, sequencing and expressing the TBP-II protein using a hypothetical TBP-II-encoding DNA molecule. A22, A25-A28. Moreover, there is no evidence in Wallach's specification that Wallach ever successfully performed any of these known protocols to identify a TBP-II encoding DNA molecule. Thus, while the majority of Wallach's specification focuses on isolating, purifying and characterizing the naturally-occurring TBP-II protein from a source in nature, *i.e.*, in human urine, Wallach's claims are directed to a genus of DNA molecules capable of producing the protein using recombinant DNA technology. However, Wallach's specification says very little about the claimed DNA molecules to be used in these recombinant DNA techniques.

Wallach's specification provides only minimal information about the structure of the claimed TBP-II-encoding DNA molecules. Indeed, Wallach's specification is more notable for what it does not disclose, than for what it does disclose. For example, Wallach's specification does not provide the complete sequence for a single species within the claimed genus of DNA molecules. Further, Wallach's specification does not disclose the complete amino acid sequence of the TBP-II protein that the claimed DNAs are supposed to encode. In fact, as noted by the

Examiner, "[t]he amino acid sequence of TBP II was not known by applicant at the time of filing of the instant application." A356. Instead, Wallach's specification provides only a short 10-13 amino acid sequence of the 185-192 amino acids that make up the TBP-II protein, from which less than ~7% of the coding region of any species of DNA falling into the claimed genus can be predicted. A25, A41-A42. In other words, over 93% of the amino acid sequence of the TBP-II protein and, thus, over 93% of the nucleic acid sequence of the claimed DNA molecules was not known or disclosed by Wallach at the time of filing.

Likewise, Wallach's specification provides no information about any function of the claimed DNA molecules that might distinguish them from other DNAs except that they encode TBP-II protein. For example, Wallach's specification discloses no probes to which the claimed DNAs might bind under various conditions. Again, all of the functions described in the specification are the same functions recited in claim 11, *i.e.*, functions of the TBP-II protein, not of the claimed genus of DNA molecules (that encode the TBP-II protein).

D. The Examiner's Analysis

The Examiner rejected Wallach's claims under 35 U.S.C. § 112, first paragraph, for lack of written description. More specifically, the Examiner found that the claims cover a genus DNA molecules that encode naturally-occurring TBP-II

protein, but that there is no disclosure in the specification of any DNA sequence that encodes the TBP-II protein. A350. The Examiner also found that Wallach's specification fails to provide any other information that might be used to readily distinguish the claimed DNA molecules from other DNA molecules. A351. On this basis, the Examiner concluded that Wallach's specification fails to describe the claimed genus of DNA molecules, other than to state that such a genus exists. *Id.*

In response to this rejection, Wallach argued that he is entitled to claim all DNA molecules that can produce the TBP-II protein -- not because he has isolated the DNA molecules, but because he has isolated the protein. More specifically, Wallach argued that he has adequately described, and is in possession of the TBP-II protein based on his disclosure of the partial amino acid sequence (*i.e.*, 10 of the 185-192 amino acids that make up the TBP-II protein) and other identifying characteristics of the protein. *See, e.g.*, A315. According to Wallach, if he possesses the TBP-II protein, then he also must possess all of the DNA molecules that encode the TBP-II protein because, according to Wallach, their sequences are an inherent property of the protein. *Id.* Wallach's argument is based upon two premises: (1) the amino acid sequence of a protein is an inherent property of the protein, and (2) the genus of nucleic acid sequences encoding a protein can be deduced based upon the amino acid sequence of the protein. *See* A304. Thus, according to Wallach, even in the absence

of either a complete amino acid sequence for the TBP-II protein or the complete nucleic acid sequence of any DNA molecule encoding TBP-II protein, Wallach's specification inherently describes the claimed DNA molecules because it describes the TBP-II protein.

The Examiner rejected Wallach's argument because "the nucleic acid encoding a protein is not an inherent property of the protein." A356 (emphasis added). The Examiner pointed out that "[w]hile the amino acid sequence of TBP II is an inherent property, in order to determine the nucleic acid sequence based on said sequence, disclosure of said sequence is required as is the actual conversion of the amino acid sequence data into appropriate nucleotides (e.g. codons) encoding said protein." A355-A356. The Examiner reasoned that, because "[t]he amino acid sequence of TBP II [protein] was not known by applicant at the time of filing of the instant application," no conversion of the amino acid sequence into nucleic acid sequence data could have taken place. A356. The Examiner then concluded that Wallach had neither conceived nor possessed the claimed DNA molecules, and that Wallach's proposed "syllogism would at best attempt to explain why the claimed nucleic acid is obvious in view of the inherent amino acid sequence of the TBP II protein." A351, A356-A357.

The Examiner also cautioned that, if Wallach's argument were accepted, the result would be "clearly repugnant to currently accepted biotechnology patent practice" because "a disclosure of an isolated protein . . . would constitute prior art under 35 U.S.C. 102 with regards to a claim reading on a nucleic acid encoding said protein." A356 (emphasis original). In other words, Wallach's line of reasoning is inconsistent with the current state of the law, which permits patents for DNA molecules that encode a given protein when the protein is known in the prior art.

E. The Board's Decision

The Board affirmed the Examiner's rejection of all claims for lack of adequate written support in Wallach's specification. More specifically, the Board agreed with the Examiner that representative claim 11 recites a "genus of DNA molecules" that comprise "a contiguous nucleotide sequence 'coding for' TBP-II." A5-6. The Board found that, in contrast to the relative breadth of claim 11, Wallach's specification fails to describe with a reasonable degree of specificity even "one species of a contiguous nucleotide sequence supporting the genus of DNA molecules covered by claim 11." A5-6. The Board also noted Wallach's admission that his specification also fails to disclose "a complete amino acid sequence of the TBP-II protein," information from which the nucleotide sequences of the claimed DNA molecules could be predicted. A6. On the foregoing, the Board concluded that "[w]here, as

here, not one species within the scope of claim 11 is described in the specification . . . applicants fall short of describing the genus of DNA molecules covered by claim 11." A5-6 (emphasis added).

The Board also specifically rejected Wallach's argument that the partial amino acid sequence for TBP-II protein (*i.e.*, 10 of 185-192 amino acids, or ~7%) and other identifying characteristics of the TBP-II protein disclosed in Wallach's specification adequately describe the claimed DNA molecules. Specifically, the Board found that the only functional information Wallach's specification provides about the claimed DNA molecules is that they "code for" TBP-II protein. A6. The Board further found that, although claim 11 is "couched in functional" terms, "the functional description of [the claimed] DNA[molecules] in applicants' specification is not enough to comply with the statute." *Id.* Accordingly, the Board held that the functional description of DNA provided in Wallach's claims and specification "does not convey to any person skilled in the art which particular DNA has been invented" because merely "acknowledging the presence of DNA . . . encoding TBP-II . . . does not constitute a sufficiently specific written description of any DNA." *Id.*

The Board further rejected Wallach's proposed syllogism, holding that relevant principles of patent law "require that genetic material be supported in the original specification by a written description containing a relatively high degree of

specificity." A5. The Board's holding is based on the principle that patent applicants claiming chemical compounds must provide enough information about those compounds to distinguish them from other materials, as enunciated by this Court in *Amgen v. Chugai Pharm. Co.*, 927 F.2d 1200, 1206 (Fed. Cir. 1991); *Fiers v. Revel*, 984 F.2d 1164, 1170-71 (Fed. Cir. 1993); and *Regents of Univ. of Cal. v. Eli Lilly & Co.*, 119 F.3d 1559, 1568 (Fed. Cir. 1997). A6-8. The Board also noted its belief that this Court's decision in *Enzo Biochem., Inc. v. Gen-Probe, Inc.*, 323 F.3d 956 (Fed. Cir. 2002), which was decided after the appeal to the Board was briefed, but before both Wallach's hearing and when the Board reached its final decision, "adheres to the to the principles of law enunciated in *Amgen*, *Fiers*, and *Eli Lilly*." A9.

IV. SUMMARY OF THE ARGUMENT

It is undisputed that Wallach's representative claim 11 covers a broad genus that includes every one of the millions of DNA molecules capable of encoding the TBP-II protein. Unfortunately, Wallach's disclosure falls far short of the broad scope of claim 11 given that it does not disclose a single DNA molecule within the scope of the claim. In fact, Wallach's disclosure does not even disclose the entire sequence of the TBP-II protein that the claimed genus of DNA molecules encode. Instead, Wallach's specification discloses only ~7% of the amino acid sequence of the TBP-II protein (*i.e.*, 10-13 of 185-192 amino acids total), from which only ~7%

of the nucleic acid sequence of any DNA molecule in the claimed genus may be predicted. Thus, the only structural limit on the claimed DNA molecules recited in representative claim 11 is that they must include one of the 30 nucleotide sequences predicted to encode the first 10 amino acids of the TBP-II protein recited in the claims. The claims provide no information about the structure of the remaining 93% of the claimed DNA molecules that encodes the other 175-182 amino acids that are estimated to make up the rest of the TBP-II protein. Similarly, the only function of the claimed DNA molecules recited in claim 11 is the naked description that they "code for" the TBP-II protein.

Wallach has isolated a naturally-occurring protein, but Wallach has not disclosed a single way to make this protein using the recombinant DNA molecules he now claims. Wallach's specification tells the public nothing more about the claimed DNA molecules than those properties recited in representative claim 11. Wallach's specification does not provide the complete sequence for a single species within the claimed genus of DNA molecules. Further, Wallach's specification does not and could not disclose the complete amino acid sequence of the TBP-II protein that the claimed DNAs are supposed to encode because that information was not known at the time of filing. Instead, Wallach's specification provides only a short 10-13 amino acid sequence of the TBP-II protein, from which less than 7% of the coding region

of any species of DNA falling into the claimed genus can be predicted. The Board properly concluded that this limited disclosure does not support the broad claims on appeal. Wallach's proposed syllogism fails to cure this deficiency.

As correctly noted, the error in Wallach's primary argument is that "the nucleic acid encoding a protein is not an inherent property of the protein." A356 (emphasis added). Moreover, if Wallach's reasoning were accepted, the result would be contrary to currently accepted biotechnology patent principles because it would mean that the disclosure of an isolated protein would be prior art under 35 U.S.C. § 102 with respect to claims directed to any nucleic acid encoding the protein. Put another way, if Wallach's argument were accepted, then every time someone isolated a protein in nature, that person would then be entitled to patent claims to every DNA molecule that could be used to genetically manufacture that protein without ever having any knowledge of those DNA molecules. If that were true, there would be no incentive for any inventor to develop materials and methods for the production of proteins using recombinant DNA techniques. Not surprisingly, this is not the current state of the law. This argument was properly rejected.

Finally, the Board properly considered the functional descriptions in Wallach's specification. However, most of the functional language in claim 11 and Wallach's specification is directed to the TBP-II protein, not to the claimed DNA

molecules (that encode the TBP-II protein). Further, the only functional information in Wallach's specification about the claimed DNA molecules is that they "code for" the TBP-II protein. As noted by the Board, this statement provides no more information about DNA molecules other than that they exist. Accordingly, Wallach's limited disclosure fails to adequately describe the claimed genus, under any articulation of the legal test for written description by this Court.

V. ARGUMENT

A. Standard Of Review

Wallach has the burden of showing that the Board committed reversible error. *In re Caveney*, 761 F.2d 671, 674 (Fed. Cir. 1985). Compliance with the written description requirement is a question of fact. *See, e.g., Hyatt v. Boone*, 146 F.3d 1348, 1352, (Fed. Cir. 1998) (relying on *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563 (Fed. Cir. 1991)); *Waldemar Link, GmbH & Co. v. Osteonics Corp.*, 32 F.3d 556, 558 (Fed. Cir. 1994). The Board's factual determinations must be upheld unless they are not supported by substantial evidence. *In re Gartside*, 203 F.3d 1305, 1316 (Fed. Cir. 2000). This Court has defined substantial evidence as that which "a reasonable mind might accept as adequate to support a conclusion":

> Substantial evidence is more than a mere scintilla. It means such relevant evidence as a reasonable mind might accept as adequate to support a conclusion . . . Mere uncorroborated hearsay or rumor does not constitute substantial evidence.

Id. at 1312 (quoting *Consolidated Edison Co. v. NLRB*, 305 U.S. 197, 229 (1938)). The Supreme Court has stated that "the possibility of drawing two inconsistent conclusions from the evidence does not prevent an administrative agency's finding from being supported by substantial evidence." *Consolo v. Federal Maritime Comm'n*, 383 U.S. 607, 620 (1966).

B. Substantial Evidence Supports The Board's Finding That Wallach's Specification Does Not Adequately Support The Broad Genus Of DNAs Covered By Representative Claim 11

The written description requirement demands that patent applicants define their inventions so as to distinguish them from other materials. *See, e.g., Fiers v. Revel*, 984 F.2d 1164, 1170-71 (Fed. Cir. 1993) (discussing *Amgen, Inc. v. Chugai Pharm. Co*, 927 F.2d 1200, 1206 (Fed. Cir. 1991). This Court has held that, for applicants claiming chemical compounds such as DNA molecules, a certain degree of specificity is generally required to make the necessary distinction between the claimed molecules and other similar molecules. *Fiers*, 984 F.2d at 1170-71. The degree of specificity that will typically satisfy the written description requirement for claims to DNA molecules includes "a precise definition, such as by structure, formula, chemical name, or physical properties." *Id.* Functional descriptions of DNA molecules may also satisfy the written description requirement provided that

the disclosed functions are known in the art to be "sufficiently correlated to a particular, known structure." *Moba, B.V. v. Diamond Automation, Inc.*, 325 F.3d 1306, 1320 (Fed. Cir. 2003) (citing *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1332 (Fed. Cir. 2003)).

Further, where a genus of DNA molecules is claimed, a representative number of species within the genus must be described in accordance with these criteria to satisfy the written description requirement. *See Regents of Univ. of Calif. v. Eli Lilly & Co.*, 119 F.3d 1559, 1566 (Fed. Cir. 1997). However, a generic statement that a genus of DNA molecules encodes a particular protein "without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others . . . it is only an indication of what the [genus of DNA molecules] does, rather than what it is." *Eli Lilly*, 119 F.3d at 1568 (emphasis added); *see also Enzo Biochem, Inc. v. Gen-Probe, Inc.*, 323 F.3d 956, 968 (Fed. Cir. 2002) ("A description of what a material does, rather than of what it is, usually does not [satisfy the written description requirement].").

1. Wallach Claims A Broad Genus Of DNA Molecules That Encode The TBP-II Protein

The Board found that representative claim 11 broadly covers a genus of DNA molecules that comprise "a contiguous nucleotide sequence 'coding for' TBP-II."

A5-6. The only limit on the genus of DNA molecules recited in claim 11 is that they encode a naturally-occurring TBP-II protein having a specific 10 amino acid sequence at one end (*i.e.,* the N terminus). Thus, the genus encompassed by representative claim 11 is limited only by the short (*i.e.*, 30 nucleotide) portion of the claimed DNA molecules that can be predicted to code for the first 10 amino acids of the TBP-II protein recited in the claims.

Claim 11 is silent about the portion of the claimed DNA molecules that encodes the other 175-182 amino acids that are estimated to make up the rest of the mature, full-length TBP-II protein. The claims are similarly silent about the structure of any other portions of the claimed DNA molecules that would not appear in the mature, full-length TBP-II protein, but which may be necessary for proper expression of the TBP-II protein, *e.g.*, a signal sequence.

Likewise, although the claims provide functional information about the TBP-II protein, they do not do so for the claimed DNA molecules, which are separate and chemically distinct from the TBP-II protein. Wallach has failed to demonstrate any correlation between the recited properties of the TBP-II protein and the structure of the claimed DNA molecules. Thus, the functional properties of the TBP-II protein recited in claim 11 do not limit the claimed DNA molecules because they do not provide any characteristic information about the claimed DNA molecules.

2. Wallach's Specification Does Not Support The Broad Genus Of DNA Molecules Encompassed By Representative Claim 11 Because It Does Not Disclose A Single Species Within The Claimed Genus And Discloses Only ~7% Of The Amino Acid Sequence Of The Protein That The Claimed DNA Molecules Encode

Wallach's specification is directed generally to the TBP-II protein, not to the claimed DNA molecules. All of the working examples in Wallach's specification are limited to the naturally-occurring TBP-II protein, *e.g.*, isolating and purifying the TBP-II protein, characterizing the purified protein, producing antibodies against the purified protein, etc. A37-A54. In contrast, there are no working examples showing a single DNA molecule that can encode the TBP-II protein. Instead, Wallach's specification contains only generic descriptions of how one might go about cloning, sequencing and expressing the TBP-II protein using a hypothetical TBP-II-encoding DNA molecule encompassed by claim 11. A22, A25-A28.

Ultimately, Wallach's specification provides only scant, partial information about the structure of the claimed DNA molecules. As noted by the Board, Wallach's specification does not provide the complete nucleic acid sequence for a single species within the claimed genus of DNA molecules. A5. Further, Wallach's specification does not disclose the complete amino acid sequence of the TBP-II protein that the claimed DNAs are supposed to encode. In fact, Wallach's specification could not have provided this information because, as noted by the Examiner, "[t]he amino acid

sequence of TBP II [protein] was not known by applicant at the time of filing of the instant application." A356. Instead, Wallach's specification provides only a short 10-13 amino acid sequence (out of the 185-192 amino acids total) of the TBP-II protein, from which less than 7% of the coding region of any species of DNA falling into the claimed genus can be predicted. A25, A41-A42. Thus, over 93% of the coding regions of the claimed DNA molecules is left unidentified.

Likewise, Wallach's specification provides no functional information about the claimed DNA molecules that would distinguish them from other DNA molecules. As the Board correctly found, the only functional information Wallach's specification provides about the claimed DNA molecules is that they "code for" TBP-II protein. A6. The Board correctly held that, although claim 11 is "couched in functional" terms, the functional description of the claimed DNA molecules in Wallach's specification is not enough to comply with the written description requirement because merely "acknowledging the presence of DNA . . . encoding TBP-II . . . does not constitute a sufficiently specific written description of any DNA." *Id.*; *see also Eli Lilly*, 119 F.3d at 1568; and *Enzo Biochem*, 323 F.3d at 969.

In the Board's words, "[w]here, as here, not one species within the scope of claim 11 is described in the specification . . . applicants fall short of describing the genus of DNA molecules covered by claim 11." A5-6 (emphasis added); *see also Eli*

Lilly, 119 F.3d at 1566. Accordingly, substantial evidence support the Board's determination that Wallach's specification does not support the genus of claim 11 in the manner mandated by 35 U.S.C. § 112, first paragraph.

Moreover, the Board's decision fully comports with this Court's decision in *In re Deuel*, 51 F.3d 1552 (Fed. Cir. 1995). Like Wallach, Deuel had broad claims to all DNA molecules encoding a particular protein, human heparin-binding growth factor (HBGF). *Deuel*, 51 F.3d at 1556 ("Claims 4 and 6 generically encompass *all* isolated/purified DNA sequences (natural and synthetic) encoding human and bovine HBGFs."). The examiner rejected Deuel's broad claims as obvious over the combined disclosures of a partial amino acid sequence of the HBGF protein and a manual describing generic cloning techniques. This Court reversed the examiner's rejection on the basis that a partial amino acid sequence and knowledge of the genetic code do not describe the claimed DNA molecules with enough specificity to render them obvious:

> [C]laims 4 and 6 are thus tantamount to the general idea of all genes encoding the protein, all solutions to the problem. Such an idea might have been obvious from the *complete* amino acid sequence of the protein, coupled with knowledge of the genetic code, because this information may have enabled a person of ordinary skill in the art to envision the idea of, and, perhaps with the aid of a computer, even identify all members of the claimed genus. The Bohlen reference, however, discloses only a partial amino acid sequence, and thus it

> appears that, based on the above analysis, the claimed genus would not have been obvious over this prior art disclosure.

Id. (emphasis original). Thus, this Court in *Deuel* specifically recognized a claim directed to a genus of DNA molecules encoding a given protein was patentable subject matter over a disclosure of a partial amino acid sequence of that protein. Consequently, *Deuel* forecloses Wallach's position that disclosure of a partial amino acid sequence adequately describes the genus of DNA molecules encoding a particular protein. More specifically, if, as in *Deuel*, the disclosure of a partial amino acid sequence of a protein combined with knowledge of the genetic code does not render obvious claims to the DNA molecules encoding that protein, that same disclosure cannot provide adequate written support for such claims because the written description requirement requires a more specific disclosure than that necessary for an obviousness rejection. *See Lockwood v. Amer. Airlines, Inc.*, 107 F.3d 1565, 1572 (Fed. Cir. 1997); *Tronzo v. Biomet, Inc.*, 156 F.3d 1154, 1158 (Fed. Cir. 1998); and *In re Winkhaus*, 527 F.2d 637, 640 (CCPA 1975) (all holding that obviousness is not the standard for satisfaction of the written description requirement). Accordingly, Wallach's disclosure of only ~7% of the amino acid sequence combined with the knowledge in the art does not even render claim 11

obvious, let alone provide adequate written support as required by 35 U.S.C. § 112, first paragraph.

3. The Rejection Is Consistent With This Court's Recent Holdings On The Written Description Requirement

The Board's fact-finding here is based upon the principle put forth in *Amgen v. Chugai*, *Fiers*, and *Eli Lilly* that patent applicants claiming chemical compounds, such as the claimed DNA molecules, must provide enough information about those compounds to distinguish them from other materials. A5-7; *see also Amgen v. Chugai*, 927 F.2d at 1206; *Fiers*, 984 F.2d at 1170-71; and *Eli Lilly*, 119 F.3d at 1568. Such distinguishing information may include functional descriptions of chemical compounds where "the disclosed function is sufficiently correlated to a particular, known structure." *See Amgen v. Hoechst*, 314 F.3d at 1332. However, as this Court stated in *Enzo Biochem*, "[a] description of what a material does, rather than of what it is, usually does not suffice" to satisfy the written description requirement. *Enzo Biochem* 323 F.3d at 969. As further clarified by this Court in *Amgen v. Hoechst*, "an adequate description of claimed DNA requires a precise definition of the DNA sequence itself -- not merely a recitation of its function or a reference to a potential method for isolating it." *Amgen v. Hoechst*, 314 F.3d at 1332; *see also Moba*, 325 F.3d at 1320-1321.

Wallach erroneously asserts that the Board applied an inappropriately high standard in denying his claims. Wallach argues that this Court's recent holdings in *Enzo Biochem*, *Amgen v. Hoechst*, and *Moba* clarify that only those DNA molecules described exclusively by "a statement of function or result [do] not adequately describe [a] claimed invention." Appellants' Br. at 17-19. In light of these recent opinions, Wallach argues that the Board improperly overlooked other "relevant identifying characteristics" that Wallach's specification discloses about the claimed DNA molecules "including partial structure and other physical and/or chemical properties and functional characteristics with a known or disclosed correlation between function and structure." Appellants' Br. at 19. However, Wallach's contention is without merit because it overstates the content of his disclosure.

The key to the Board's finding is that the generic functional description of the claimed DNA molecules provided in Wallach's disclosure is not correlated with the structures of any claimed DNA molecules that perform the recited function. More specifically, the Board expressly found that the only function recited in Wallach's specification for the claimed DNA molecules is that they "code for" the TBP-II protein. A6. Wallach's specification fails to disclose any other functions of the claimed DNA molecules that might convey to those skilled in the art which particular DNA molecules Wallach is claiming. For example, Wallach's specification discloses

no probes to which the claimed DNA molecules might bind under specific conditions. Accordingly, the Board properly found that, "the functional description in applicants' specification is not enough to comply with the statute" because it merely "acknowledg[es] the presence of DNA serving a particular function (encoding TBP-II)" without conveying to any person skilled in the art which particular DNA has been invented. A6. Thus, the Board did not hold that a functional description of a DNA is not enough to comply with the written description requirement. The Board simply found that the functional description provided in Wallach's specification was not enough to comply with the written description requirement. *Id.*[4]

Moreover, Wallach has yet to specifically identify any "relevant identifying characteristics" of the claimed DNA molecules disclosed in Wallach's specification that the Board overlooked in its decision. The same can be said of the "other physical and/or chemical properties and functional characteristics with a known or disclosed correlation between function and structure" that Wallach complains the Board overlooked. For all these reasons, the Board's ultimate determination that the partial amino acid sequence and functional description of the claimed DNA molecules actually provided in Wallach's specification (*i.e.*, "coding for" TBP-II protein) fails

[4] The Board's exact words were, "the functional description of DNA in applicants'

to satisfy the written description requirement is entirely consistent with this Court's recent holdings in *Enzo Biochem*, *Amgen v. Hoechst*, and *Moba*.

Lastly, it is important to note that if Wallach believed that the *Enzo* decision signaled a change in how the written description requirement is applied, Wallach could have argued this point to the Board at his hearing.[5] Further, if Wallach believed that either the *Enzo* or the *Amgen v. Hoechst* decisions exposed an error in the Board's legal reasoning, Wallach should have asked for rehearing by the Board under 37 C.F.R. § 1.197(b) in view of any clarification of the law.[6] Instead, Wallach appealed the Board's decision directly to this Court.

4. Wallach's Proposed Syllogism Fails To Make Up For The Deficiencies Of Wallach's Specification

In an attempt to compensate for the lack of explicit disclosure in his application, Wallach offers the following syllogism to overcome the present rejection. Appellants' Br. at 14-15. Wallach argues that because a claim directed to the TBP-II protein was allowed in one of his other applications that has the same specification as Wallach's specification (*i.e.*, U.S. Serial No. 07/930,443), Wallach's

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specification is not enough to comply with the statute." A6 (emphasis added).

[5] *Enzo Biochem* was decided on July 15, 2002. Wallach's hearing took place on August 27, 2002.

6 The Board's decision issued on December 26, 2002. This Court's decision in *Amgen v. Hoechst* issued eleven days later, on January 6, 2003. Thus, Wallach had the option to seek rehearing by the Board up until February 26, 2003. *See* 37 C.F.R.

specification must adequately describe the TBP-II protein. *Id.*; *see also* Br. at 12, ¶12, and 26. Wallach further argues that, because Wallach's specification is presumed to adequately describe the TBP-II protein, then it must also adequately describe the claimed DNA molecules. *Id., see also* Br. at 26-27. Wallach's argument is based upon two premises: (1) the amino acid sequence of a protein is an inherent property of the protein, and (2) the nucleic acid sequence encoding a protein can be deduced based upon the amino acid sequence of the protein. Thus, according to Wallach, even in the absence of either a complete amino acid sequence for the TBP-II protein or a single complete nucleic acid sequence of any DNA molecule encoding TBP-II protein, Wallach's specification inherently describes the claimed DNA molecules because it describes the TBP-II protein. In short, Wallach argues that any person who isolates a protein found in nature also has possession of every DNA molecule capable of encoding that protein, even though that person has not described a single such DNA molecule!

The error in Wallach's argument is that "the nucleic acid encoding a protein is not an inherent property of the protein." A356 (emphasis added). Consistent with this Court's observations in *Deuel*, in order to determine the nucleic acid sequence of the claimed DNA molecules based upon the amino acid sequence of the TBP-II

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§ 1.197(b).

protein, a "disclosure of the [TBP-II protein's amino acid] sequence is required as is the actual conversion of the amino acid sequence data into appropriate nucleotides (*e.g.* codons) encoding said protein." A355-A356; *see also Deuel*, 51 F.3d at 1560. Further, because "[t]he amino acid sequence of TBP II [protein] was not known by applicant at the time of filing of the instant application," no conversion of the amino acid sequence into nucleic acid sequence data could have taken place. A356.

More importantly, if Wallach's reasoning were accepted, the disclosure of an isolated protein (with an appropriate publication date) would now constitute prior art under 35 U.S.C. § 102 with respect to claims reading on the DNA molecules encoding the protein. Put another way, if Wallach's argument were accepted, then every time someone isolated a protein in nature, that person would then be entitled to patent claims to every DNA molecule that could be used to genetically manufacture that protein without ever having any knowledge of those DNA molecules. If that were true, there would be no incentive for any inventor to develop materials and methods for the production of proteins using recombinant DNA techniques. Not surprisingly, this is not the current state of the law.

For example, in *Amgen v. Chugai*, 927 F.2d 1200 (Fed. Cir. 1991), this Court concluded that claims directed to DNA molecules encoding the erythropoietin protein (EPO) were not anticipated by the disclosure of partial sequences of two

regions of the EPO gene, probes to those regions and a general cloning strategy. However, if Wallach's argument is accepted, these same claims would not only be anticipated by the aforementioned disclosure, but also by the prior art disclosure of the EPO protein isolated from human urine. Likewise, claims to DNA molecules encoding known, isolated proteins in at least two other cases that this Court concluded were not invalid or obvious over various prior art, would now be held anticipated or obvious. *See, e.g., Deuel*, 51 F.3d at 1555-56 (Fed. Cir. 1995) (claims to DNAs encoding HBGFs would be anticipated by the prior art disclosure of HBBMs by Bohlen); *Fiers*, 984 F.2d at 1168 n.9 (Fed. Cir. 1993) (claims to DNAs encoding β-interferon (β-IFN) would be anticipated by the prior art disclosure of the first 13 amino acids of β-IFN); *see also Eli Lilly*, 119 F.3d at 1562 (claims to DNAs encoding *human* insulin would now be anticipated by the prior art disclosure of human insulin). Thus, as the Examiner correctly noted, this result would be "clearly repugnant to currently accepted biotechnology patent practice." A356 (emphasis original).

Moreover, one must ask the obvious question: if, as Wallach asserts, it is such a trivial matter to deduce the DNA molecule that encodes a given protein once that protein has been isolated, why hasn't Wallach done so? The question answers itself: because it is not so easy, and even more difficult in this case because Wallach has

identified only ~7% of the amino acid sequence of the protein that the claimed genus of DNA molecules encode. For all these reasons, after carefully considering Wallach's syllogism, the Board properly rejected it as inconsistent with the relevant principles of patent law. A5.

CONCLUSION

If allowed, Wallach's claimed genus would cover every one of the millions of DNA molecules that can encode the TBP-II protein. However Wallach's specification does not support the broad claims on appeal in the manner required by 35 U.S.C. § 112, first paragraph, because, *inter alia*, it does not disclose a single species of DNA molecule within the broad claimed genus, and it discloses only ~7% of the amino acid sequence of the protein the genus encodes. Because the Board's fact-finding is supported by substantial evidence this Court should affirm the present rejection.

Respectfully submitted,

September 30, 2003

JOHN M. WHEALAN
Solicitor

MARY L. KELLY
RAYMOND T. CHEN
Associate Solicitors

P.O. Box 15667
Arlington, Virginia 22215
(703) 305-9035
Attorneys for the Director of the United States Patent and Trademark Office

RULE 32(A)(7)(C) CERTIFICATE OF COMPLIANCE

I certify pursuant to FRAP 32(a)(7) that the foregoing brief complies with the type-volume limitation. The total number of words, excluding the table of contents and table of authorities, as calculated by the Word 2000® software program is 6,839.

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Cold Spring Harbor, New York

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Front cover (paperback): The gene encoding green fluorescent protein was cloned from *Aequorea victoria*, a jellyfish found in abundance in Puget Sound, Washington State. This picture of a 50-mm medusa was taken on color film by flash photography and shows light reflected from various morphological features of the animal. The small bright roundish blobs in the photograph are symbiotic amphipods living on or in the medusa. The bright ragged area in the center is the jellyfish's mouth.

Bioluminescence from *Aequorea* is emitted only from the margins of the medusae and cannot be seen in this image. Bioluminescence of *Aequorea*, as in most species of jellyfish, does not look like a soft overall glow, but occurs only at the rim of the bell and, given the right viewing conditions, would appear as a string of nearly microscopic fusiform green lights. The primary luminescence produced by *Aequorea* is actually bluish in color and is emitted by the protein aequorin. In a living jellyfish, light is emitted via the coupled green fluorescent protein, which causes the luminescence to appear green to the observer.

The figure and legend were kindly provided by Claudia Mills of the University of Washington, Friday Harbor. For further information, please see Mills, C.E. 1999–2000. Bioluminescence of *Aequorea*, a hydromedusa. Electronic Internet document available at http://faculty.washington.edu/cemills/Aequorea.html. Published by the author, web page established June 1999, last updated 23 August 2000.

Back cover (paperback): A portion of a human cDNA array hybridized with a red fluor-tagged experimental sample and a green fluor-tagged reference sample. Please see Appendix 10 for details. (Image provided by Vivek Mittal and Michael Wigler, Cold Spring Harbor Laboratory.)

Library of Congress Cataloging-in-Publication Data

Sambrook, Joseph.
Molecular cloning : a laboratory manual / Joseph Sambrook, David W. Russell.-- 3rd ed.
p. ; cm.
Includes bibliographical references and index.
ISBN 0-87969-576-5 (cloth) -- ISBN 0-87969-577-3 (pbk)
1. Molecular cloning--Laboratory manuals.
[DNLM: 1. Cloning, Molecular--Laboratory Manuals. QH 440.5 S187m 2001] I. Russell, David W. (David William), 1954- . II. Title.
QH442.2 .S26 2001
572.8--dc21

00-064380

10 9 8 7 6 5 4 3 2 1

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2nd position of codon

1st position of codon (5′ terminus)	U	C	A	G	3rd position of codon (3′ terminus)
U	UUU Phe	UCU Ser	UAU Tyr	UGU Cys	U
	UUC Phe	UCC Ser	UAC Tyr	UGC Cys	C
	UUA Leu	UCA Ser	UAA Stop (Ochre)	UGA Stop	A
	UUG Leu	UCG Ser	UAG Stop (Amber)	UGG Trp	G
C	CUU Leu	CCU Pro	CAU His	CGU Arg	U
	CUC Leu	CCC Pro	CAC His	CGC Arg	C
	CUA Leu	CCA Pro	CAA Gln	CGA Arg	A
	CUG Leu	CCG Pro	CAG Gln	CGG Arg	G
A	AUU Ile	ACU Thr	AAU Asn	AGU Ser	U
	AUC Ile	ACC Thr	AAC Asn	AGC Ser	C
	AUA Ile	ACA Thr	AAA Lys	AGA Arg	A
	AUG Met	ACG Thr	AAG Lys	AGG Arg	G
G	GUU Val	GCU Ala	GAU Asp	GGU Gly	U
	GUC Val	GCC Ala	GAC Asp	GGC Gly	C
	GUA Val	GCA Ala	GAA Glu	GGA Gly	A
	GUG Val	GCG Ala	GAG Glu	GGG Gly	G

FIGURE A7-1 The Genetic Code

CERTIFICATE OF SERVICE

I certify that on September 30, 2003, I caused two copies of the foregoing BRIEF FOR APPELLEE - DIRECTOR OF THE UNITED STATES PATENT AND TRADEMARK OFFICE to be transmitted via Express Mail to the following address:

Roger L. Browdy
BROWDY & NEIMARK, PLLC
624 Ninth St. NW
Washington, DC 20001

Mary L. Kelly
Associate Solicitor

ADDENDUM

Wallach's specification does not teach any function of the claimed DNA molecules except the naked recitation that they encode the TBP-II protein. Wallach's specification fails to provide any other information from which the claimed DNA molecules might be distinguished from other DNA molecules. Because of these deficiencies, the Board found that Wallach's specification lacks adequate written support for the broadly claimed genus of DNA molecules encompassed by representative claim 11. Thus, the sole issue on appeal is whether substantial evidence supports the Board's factual finding that Wallach's specification does not describe the claimed genus of DNA molecules in the manner required by 35 U.S.C. § 112, first paragraph.

II. STATEMENT OF THE CASE

This is an appeal from a decision of the Board of Patent Appeals and Interferences (the "Board") of the United States Patent and Trademark Office ("USPTO") affirming the final rejection of claims 11-13, 35-38, 43-44, 46-49, 51-54, 56-61, and 63-64 of U.S. Serial No. 08/485,129 ("Wallach's specification") under 35 U.S.C. § 112, first paragraph, for lack of written description. A1-A11.[1] The appellants (hereinafter "Wallach") have stated before the Board that all claims on

[1] Citations to Appellants' Brief will be referred to as "Appellants' Br. at __," and citations to the Joint Appendix as "A__."

2nd position of codon

1st position of codon (5′ terminus)	U	C	A	G	3rd position of codon (3′ terminus)
U	UUU Phe	UCU Ser	UAU Tyr	UGU Cys	U
	UUC Phe	UCC Ser	UAC Tyr	UGC Cys	C
	UUA Leu	UCA Ser	UAA Stop (Ochre)	UGA Stop	A
	UUG Leu	UCG Ser	UAG Stop (Amber)	UGG Trp	G
C	CUU Leu	CCU Pro	CAU His	CGU Arg	U
	CUC Leu	CCC Pro	CAC His	CGC Arg	C
	CUA Leu	CCA Pro	CAA Gln	CGA Arg	A
	CUG Leu	CCG Pro	CAG Gln	CGG Arg	G
A	AUU Ile	ACU Thr	AAU Asn	AGU Ser	U
	AUC Ile	ACC Thr	AAC Asn	AGC Ser	C
	AUA Ile	ACA Thr	AAA Lys	AGA Arg	A
	AUG Met	ACG Thr	AAG Lys	AGG Arg	G
G	GUU Val	GCU Ala	GAU Asp	GGU Gly	U
	GUC Val	GCC Ala	GAC Asp	GGC Gly	C
	GUA Val	GCA Ala	GAA Glu	GGA Gly	A
	GUG Val	GCG Ala	GAG Glu	GGG Gly	G

The Genetic Code